SPIRIT | CONSORT SURROGATE
Reporting Guidelines for Surrogate Endpoints

The box below gives a glossary of terminology used in the SPIRIT-SURROGATE and CONSORT-SURROGATE checklists.

Although we have provided a definition for "surrogate endpoints", you will have a chance to rank various definitions of surrogate endpoints after rating the items

Surrogate endpoint: A biomarker or intermediate outcome used to substitute for a patient or participant relevant final outcome (i.e., variable that captures how an individual feels, functions, or how long they survive) and predicts benefit or harm based on epidemiologic, therapeutic, pathophysiologic, or other scientific evidence Examples include blood pressure for cardiovascular events such as stroke and heart attacks
Biological marker (biomarker): a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are types of biomarkers. A biomarker is not an assessment of how an individual feels, functions, or survives." (http://www.ncbi.nlm.nih.gov/books/NBK326791/) Examples include tumour size in cancer, blood pressure in stroke and heart attacks, blood sugar in diabetes, viral load in HIV
Intermediate outcome: an endpoint measuring an outcome that can be measured earlier than an effect on final outcome and that is considered reasonably likely to predict the interventions effect on final outcome (http://www.ncbi.nlm.nih.gov/books/NBK326791/) Examples include fruit and vegetable intake in trials of prevention of cardiovascular events; exercise tolerance in trials of device treatments for heart failure; progression free survival for overall survival in cancer
Patient or participant relevant final outcome also referred to as clinical endpoint, patient centred outcome or final outcome**:** a measurement that reflects how an individual feels, functions, or survives. It is thought to be the most credible measurement when assessing the risks and benefits of interventions. (https://jamanetwork.com/journals/jama/fullarticle/2762451) Examples include mortality, health-related quality of life, and major morbidity (e.g. hospitalisation)
Surrogate primary endpoint: A surrogate endpoint used as the primary outcome(s) in a trial
Primary outcome: the outcome that an investigator considers to be the most important among the many outcomes that are to be examined in the study. (https://www.psychiatrist.com/jcp/assessment/research-methods-statistics/primary-outcome-measure-importance-clinical-trials/)

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CONSORT (Consolidated Standards of Reporting Trials) a checklist used to report completed trials. (http://www.consort-statement.org/)
CONSORT-SURROGATE: a modified CONSORT checklist that will be used to report randomised controlled trials using surrogate primary endpoints
Composite outcome: an outcome consisting of two or more component outcomes (e.g., proportion of participants who died or experienced a nonfatal stroke). Participants who have experienced any one of the events specified by the components are considered to have experienced the composite outcome (https://www.sciencedirect.com/science/article/pii/S0895435606004938)
Randomised controlled trial (RCTs): studies that randomly assign a number of similar people to two or more groups to test the benefits of an intervention for example drug or treatment.
SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) a checklist used to report randomised controlled trial protocols (detailed plan of the trial) (http://www.spirit-statement.org/)
SPIRIT-SURROGATE: modified SPIRIT checklist that will be used to report randomised controlled trial protocols using surrogate primary endpoints
Surrogate threshold effect (STE) is the minimum surrogate endpoint effect that predicts a health benefit. For example, a reduction of 7.1 mmHg for systolic blood pressure and 2.4 mmHg for diastolic blood pressure predicts a stroke reduction benefit (https://pubmed.ncbi.nlm.nih.gov/22409774/)
Validation: process to determine whether the effect on the surrogate predicts the effect on the intended final outcome. A validated surrogate endpoint is supported by a biological plausibility rationale and/or statistical confirmation of a strong association between trial treatment effect on the surrogate outcome and treatment effect on patient/participant relevant final outcome. For example, blood pressure reduction is a validated surrogate endpoint for reduction of stroke and heart attacks; blood sugar reduction (HbA1c) is a validated surrogate for certain diabetes related complications; uric acid reduction is a validated surrogate endpoint for improvement of gout symptoms (http://www.ncbi.nlm.nih.gov/books/NBK326791/)